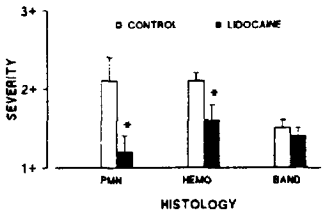

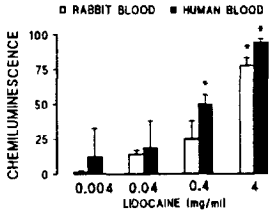

Conclusions; (i) The beneficial effect of lido on infarct size was associated with a significant reduction in the accumulation of PMNs in the reperfused rabbit myocardium. (ii) This beneficial effect may occur as a direct inhibitory effect of lido on PMNs. (iii) This effect of lido on infarct size may also occur in man as human cells respond similarly in vitro to equal doses of lidocaine. (iiii) Lidocaine may confound the interpretation of other interventions to reduce infarct size in animals and possibly in man.

923-2 Effects of L-Carnitine on Left Ventricular Function After Acute Myocardial Infarction. Results of the CEDIM (Carnitina Ecocardiografia Digitale Infarto Miocardico) Trial

Sabino Iliceto, Vito Marangelli, Giuseppe Santoro, Luca Boni, Gaetano D'Ambrosio, Domenico Scrutinio, Paolo Bruzzi, Paul G. Hugenholtz, Paolo Rizzon, CEDIM Investigators. *Institute of Cardiology, Bari, Italy*

Limitation of left ventricular (LV) dilatation (LV remodeling) after acute myocardial infarction (AMI) has become an essential therapeutic goal since the entity of LV dilatation after AMI is now recognized to be the most powerful prognostic predictor for clinical outcome. L-Carnitine (L-C) is an essential compound of cardiac metabolism that favours the optimal utilization of energetic substrates. Experimental studies have demonstrated that L-C administration during and after myocardial ischemia restores L-C cardiac depletion following ischemia and exerts a beneficial effect on LV function. To test the hypothesis, that timely restoration of adequate intracardiac L-C levels after AMI could limit LV dilatation on a long-term basis in a clinical setting, a multicenter, randomized, double-blind, placebo controlled trial was undertaken (CEDIM trial). 472 pts with first, anterior AMI and high quality entry 2D echo were enrolled (370/472 pts underwent thrombolysis). Pts were randomized to placebo (PI) or L-C (6 g/day iv for the first 5 days and 9 g/day orally for the following 12 months). 2D echo was digitally performed on admission, at 3, 6, 12 months after AMI. 2D echo images were transmitted via modem using a long-distance network to a Core Laboratory where end-diastolic and end-systolic volumes (EDV, ESV) were assessed. Baseline clinical and echocardiographic characteristics were similar in L-C and PI groups. Percent variation (Δ %) of EDV and ESV at 3, 6, 12 months from baseline was evaluated in both PI and L-C groups.

Results:		3 months	6 months	12 months
Δ%-EDV	L-C	11.1 ± 30.2	12.7 ± 26.8	19.1 ± 36.2
	PI	18.0 ± 33.0*	19.5 ± 30.6*	28.5 ± 40.2*
Δ%-ESV	L-C	12.6 ± 41.6	15.1 ± 36.8	28.9 ± 51.4
	PI	22.5 ± 42.8*	25.6 ± 42.3**	39.9 ± 55.1*

*p < 0.05, **p = 0.01 (Student's t test L-C vs PI)

Congestive heart failure developed in 10 pts (4.2%) on PI vs 4 pts (1.7%) on L-C. *Conclusion;* Timely administration of L-C after AMI limits LV dilatation in the first year after AMI and, therefore, represents a new approach to optimize LV remodeling after AMI.

923-3 Fluosol Reduces Myocardial Reperfusion Injury by Prolonged Suppression of Neutrophils by its Detergent Component (RheothRx) and not by Enhancing O_2 Delivery

João V. Vitola, David A. Ingram, John P. Holsinger, James B. Atkinson, Mervyn B. Forman, John J. Murray. *Vanderbilt University, Nashville, TN*

Fluosol, a complex mixture of O_2 carrying perfluorocarbons (PFCs) emulsified by the detergent pluronic F-68 and a variety of lipids, significantly reduces myocardial reperfusion injury (RI) in animals and humans as shown in some initial clinical trials. Potential mechanisms for Fluosol include enhanced O_2 delivery to the reperfused tissue and modulation of various neutrophil (PMNs) functions. Recent studies in dogs and man demonstrate the same beneficial effect for treatment of RI with the detergent component alone, RheothRx, which is currently undergoing clinical trials. We have shown that the effect of Fluosol on PMNs is related to this detergent. However, prolonged infusion (48 hrs) of detergent is required to reduce RI to the same extent as Fluosol given over only 1 hr. Possible mechanisms for the beneficial effects of Fluosol (O_2 delivery vs effects on PMNs) were investigated in a model of regional ischemia utilizing rabbits undergoing 30 mins of circumflex occlusion and 48 hrs of reperfusion. Infarct size (area of necrosis, AN) was determined histologically and expressed as percent of risk region (area at risk, AR). Animals received Fluosol (30 cc/kg) with or without O_2 or saline over the first 60 mins of reperfusion. AR was similar in all groups. (Mean ± SEM of AN/AR (%), n = 11 for all groups). The treatment with Fluosol with or without O_2 (44 ± 3 and 40 ± 3, respectively) was significantly ($p < 0.05$) reduced compared to control (63 ± 4). Another group received F-108, a larger size pluronic detergent found to be 2.5-fold more potent in suppressing PMN function *in vitro* compared to F-68, during the first 3 hrs of reperfusion. This treatment did not alter the infarct size (63 ± 5). RheothRx was found to form 4 nm micelles in solution whereas Fluosol formed particles approximately 100 times larger. Similar sized particles were formed by substituting the perfluorocarbons with mineral oil. The *in vitro* activity of this pluronic/mineral oil micelle on PMN function was similar to Fluosol. Infusion of these larger oil micelles was tolerated by rabbits and used in further infarct studies. *Conclusions;* These studies suggest that (1) reduction of RI by Fluosol is not due to enhanced O_2 delivery by the PFCs to reperfused myocardium and (2) since the Fluosol emulsion markedly reduces the clearance of the detergent F-68 ($t_{1/2}$: Fluosol ≅ 8 hrs vs RheothRx ≅ 1.5 hrs), prolonged PMN suppression rather than potency of suppression is the mechanism whereby Fluosol ameliorates RI. Fluosol's clinical efficacy may be enhanced by prolonging its infusion to ensure an adequate blood level to suppress PMN function beyond the time of reperfusion injury. RheothRx's clinical usefulness may be facilitated by decreasing its renal clearance by delivering larger micelles of the detergent in order to produce prolonged PMN suppression with a shorter infusion time.

923-4 Predictors of Early Recovery in Left Ventricular Function After Primary Angioplasty in Acute Myocardial Infarction

Luiz A. Mattos, Fausto Feres, Luiz F. Tanajura, Ibraim Pinto, Aurea Chaves, Marinella Centemero, Gilberto Nunes, Amanda Sousa, J. Eduardo Sousa. *Dante Pazzanese Institute of Cardiology, Sao Paulo, Brazil*

Clinical and angiographic data were analysed in 244 pts submitted to a successful primary PTCA within 24 hrs of acute MI to determine predictors of early recovery in LV function. All pts had a LV angiogram before PTCA and at hospital discharge (HD – mean = 10 days). The end points were: analysis of arterial patency rate at HD and its relation to ejection fraction (EF) recovery and in pts with sustained arterial patency (SAP), which ones exhibit a greater increase in EF. P values < 0.05 were submitted to multivariate analysis (risk adjustment).

Variable	%	Pre EF	HD EF	GAIN	P
Arterial Patency	91	43 ± 9	49 ± 8	+6.1 ± 4%	0.001*
Reocclusion	9	45 ± 8	41 ± 10	−3.4 ± 5%	
ONLY PTS WITH SAP:					
Anterior MI	52	41 ± 7	47 ± 9	+6.3 ± 4%	0.02
Inferior MI	48	49 ± 9	52 ± 10	+3.1 ± 2%	
Ischemia time < 4 hrs	42	44 ± 8	53 ± 9	+9.4 ± 5%	0.001*
Ischemia time > 4 hrs	58	44 ± 9	49 ± 5	+5.1 ± 2%	
Multivessel disease	52	42 ± 9	50 ± 7	+8.1 ± 4%	0.02
Single vessel disease	48	44 ± 10	48 ± 9	+3.9 ± 3%	
Baseline EF < 40%	43	33 ± 9	42 ± 8	+9.6 ± 5%	0.001*
Baseline EF > 40%	57	51 ± 9	54 ± 5	+3.2 ± 1%	

Conclusions; Pts with SAP* and anterior MI, multivessel disease, baseline EF < 40%* and early reperfusion* are likely to benefit most from primary PTCA in acute myocardial infarction (*independent variables).

923-5 Tissue Factor Pathway Inhibitor Decreases Myocardial Reperfusion Injury in Dogs

Christopher M. Speidel, Gerrald Galluppi [1], Dana R. Abendschein. *Washington University, St. Louis, MO;* [1] *Monsanto/Searle, St. Louis, MO*

Local administration of recombinant tissue factor pathway inhibitor (rTFPI), the physiologic inhibitor of the tissue factor-factor VIIa complex that also inhibits factor Xa, attenuates necrosis after reperfusion of ischemic ears in rab-

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